UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

TXR No. 0054532

MEMORANDUM

Date: 01-MAR-2007

Subject: DIFENOCONAZOLE (PC Code 128847). Request for Restatement of 1994 EPA Cancer Classification and Risk Assessment Approach Using Current Terminology.

DP No. 318039 MRIDs 46551700 and 46551701

From: P.V. Shah, Acting Branch Chief
Registration Action Branch 1 (RAB1)/Health Effects Division (HED) (7509P)

Thru: William Burnam, Chair,
HED Cancer Assessment Review Committee (CARC)
Health Effects Division (HED) (7509P)

To: Robert Westin/Tony Kish (RM 22)
Registration Division (RD; 7505P)

ACTION REQUESTED:

The Registration Division (RD) of the Office of Pesticide Programs (OPP) requested the HED to evaluate Syngenta's request for restatement of the 1994 EPA cancer classification and risk assessment approach using current terminology for difenoconazole (MRIDs 46551700 and 46551701).

BACKGROUND:

On May 18, 1994, the CPRC classified difenoconazole as a Group C carcinogen based on statistically significant increases in liver adenomas, carcinomas and combined

adenomas/carcinomas in both sexes of CD-1 mice, only at doses which were considered to be excessively high for carcinogenicity testing. The CPRC recommended that for the purpose of risk characterization, the margin-of-exposure (MOE) approach should be used for quantification of human risk. The MOE approach was selected because there was only very weak (limited) evidence of carcinogenic potential at doss levels not considered to be excessive, with significant changes observed only at excessive doses. In addition, there was no evidence of genotoxicity. Therefore, a threshold model was recommended for estimating risk.

In 1999, HED used linear extrapolation approach for Difenoconazole risk assessment (HED Docment No. D234002, dated March 22, 1999), since at that time, the Agency had not defined the level of concern for cancer using the MOE approach. A quantitative risk analysis was conducted utilizing the Q1* approach. The Q1* was determined to be 1.57 x 10-1 (mg/kg/day)-1. This value incorporates the 3/4 scaling factor and is based on the male mouse liver adenomas and/or carcinomas combined.

Since the EPA has used two different approaches in estimating the human health risk, Syngenta is requesting the EPA to restate and clarify the 1994 EPA cancer classification and risk assessment approach using current terminology for difenoconazole. No new data were provided by Syngenta (MRIDs 46551700 and 46551701).

CONCLUSIONS:

No new data were submitted by Syngenta. In accordance with HED's current policy and EPA's 2005 Final Guidelines for Carcinogenic Risk Assessment, difenoconazole can be classified as "Suggestive Evidence of Carcinogenic Potential." Quantification of cancer risk is not required. The RfD would address the concern for chronic toxicity, including carcinogenicity, likely to result from exposure to the pesticide.

No enclosues
CC Jessica Kidwell, Executive Secretary, CARC

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R141182

Chemical: Perchlorobenzene

PC Code:
061001

HED File Code:
Memo Date: 12/7/1987
File ID: 00000000
Accession #: 000-00-0117

HED Records Reference Center
3/8/2007